



IBW

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(Case No. 02-134-D)

In the Application of:

Lavie et al.

Serial No.: 10/791,155

Filing Date: March 1, 2004

For: Use of Specifically Engineered Enzymes  
To Enhance the Efficacy of Prodrugs

Examiner:

Group Art Unit: 1652

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

1. We are transmitting herewith the attached papers for the above-identified patent application:

- ☒ Information Disclosure Statement  
☒ PTO Form 1449 and cited references

2. **GENERAL AUTHORIZATION TO CHARGE OR CREDIT FEES:** Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490.
3. **CERTIFICATE OF MAILING UNDER 37 CFR § 1.8:** The undersigned hereby certifies that this Transmittal Letter and the papers, as described in paragraph 1 herein-above, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Alexandria VA 22313-1450 on this 5th day of January, 2006.

By:

Jason J. Derry, Ph.D.

Registration No. 50,692



**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**  
(Case No. 02-134-D)

**In the Application of:**

**Lavie et al.**

**Serial No.: 10/791,155**

**Filing Date: March 1, 2004**

**For: Use of Specifically Engineered Enzymes  
To Enhance the Efficacy of Prodrugs**

**Examiner:**

**Group Art Unit: 1652**

**INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

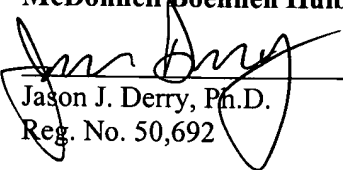
Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references of record in the above-identified application. This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. Copies of the references cited below are enclosed. These references are also listed on the enclosed PTO Form 1449.

In the judgment of the undersigned, portions of the listed references may be material to the Examiner's consideration of the presently pending claims. This statement is not a representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. Section 102 or Section 103.

Applicants do not believe any fee is due with this submission. If this belief be in error and the Patent Office determines that the fee prescribed in the relevant portion of 37 C.F.R. Section 1.97 is applicable, the undersigned representative by his signature hereby authorizes any such fee to be debited from Deposit Account 13-2490.

Respectfully submitted,  
**McDonnell Boehnen Hulbert & Berghoff**

Date: January 5, 2006

  
Jason J. Derry, Ph.D.  
Reg. No. 50,692

Substitute for form 1449A/PTO

Complete if Known

Application No.

10/791,155

Filing Date:

March 1, 2004

First Named Inventor

Lavie et al.

Group Art Unit

1652

Examiner Name

Attorney Docket No.

02-134-D

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(use as many sheets as necessary)

1

of

1

## U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. 1	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
		2001/0012835	A1	Fine et al.	08-09-2001	

## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. 1	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				

## OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. 1	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		BERGMAN <i>et al.</i> , Decreased resistance to gemcitabine (2',2'-difluorodeoxycytidine) of cytosine arabinoside-resistant myeloblastic murine and rat leukemia cell lines: role of altered activity and substrate specificity of deoxycytidine kinase, 1999, <i>Biochem. Pharmacol.</i> 57:397-406;	
		BLACKSTOCK <i>et al.</i> , Tumor uptake and elimination of 2',2'-difluoro-2'-deoxycytidine (gemcitabine) after deoxycytidine kinase gene transfer: correlation with in vivo tumor response, 2001, <i>Clin. Cancer Res.</i> 7:3263-8	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC. 20231

# OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. 1	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		BLAKEY <i>et al.</i> , "Enzyme Prodrug Therapy of Cancer" Exp. Opin. Ther. Patents (September 1997) 7(9) 966-977.	
		ESTEY <i>et al.</i> , Variables predicting response to high dose cytosine arabinoside therapy in patients with refractory acute leukemia, 1987, <i>LEUKEMIA</i> 1:580-3;	
		ESTEY, How I treat older patients with AML, 2000, <i>Blood</i> 96:1670-3	
		GANDHI <i>et al.</i> , Fludarabine potentiates metabolism of cytarabine in patients with acute myelogenous leukemia during therapy, 1993, <i>J. Clin. Oncol.</i> 11:116-24	
		GLADSTONE <i>et al.</i> , "Antibody Directed Doxycytidine Kinase (DCK) Enhances the Cytotoxicity of Ara -C Towards CD33+ Leukemia Cells. Session Type: Oral Session" Blood 102(11) 138A (November 16 2003).	
		GOAN <i>et al.</i> , Overexpression of ribonucleotide reductase as a mechanism of resistance to 2,2-difluorodeoxycytidine in the human KB cancer cell line, 1999, <i>Cancer Res.</i> 59:4204-7	
		HAPKE <i>et al.</i> , Retroviral transfer of deoxycytidine kinase into tumor cell lines enhances nucleoside toxicity, 1996, <i>Cancer Res.</i> 56:2343-7	
		HUBERT <i>et al.</i> , STEAP: a prostate-specific cell-surface antigen highly expressed in human prostate tumors, 1999, <i>Proc Natl Acad Sci U S A.</i> 7:14523-8	
		IACOBONI <i>et al.</i> , High-dose cytosine arabinoside: treatment and cellular pharmacology of chronic myelogenous leukemia blast crisis, 1986, <i>J. Clin. Oncol.</i> 4:1079-88	
		KABOURIDIS, Biological applications of protein transduction technology, 2003, <i>Trends in Biotechnology</i> 21:498-503	
		KAKIHARA <i>et al.</i> , Expression of deoxycytidine kinase (dCK) gene in leukemic cells in childhood: decreased expression of dCK gene in relapsed leukemia, 1998, <i>Leuk. Lymphoma</i> 31:405-9;	
		KANTARJIAN <i>et al.</i> , Phase I-II clinical and pharmacologic studies of high-dose cytosine arabinoside in refractory leukemia, 1986, <i>Am. J. Med.</i> 81:387-94	
		KNECHT <i>et al.</i> , 2002, A few amino acid substitutions can convert deoxyribonucleoside kinase specificity from pyrimidines to purines, <i>EMBO J.</i> 21:1873-1880	
		LOTFI <i>et al.</i> , Biochemical pharmacology and resistance to 2-chloro-2'-arabino-fluoro-2'-deoxyadenosine, a novel analogue of cladribine in human leukemic cells, 1999, <i>Clin. Cancer Res.</i> 5:2438-44;	

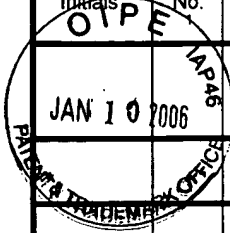
Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> Applicant is to place a check mark here if English translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC. 20231

# OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		MANSSON <i>et al.</i> , Down-regulation of deoxycytidine kinase in human leukemic cell lines resistant to cladribine and clofarabine and increased ribonucleotide reductase activity contributes to fludarabine resistance, 2003, <i>Biochem. Pharmacol.</i> <u>65</u> :237-247	
		OWENS <i>et al.</i> , Resistance to 1-beta-D-arabinofuranosylcytosine in human T-lymphoblasts mediated by mutations within the deoxycytidine kinase gene, 1992, <i>Cancer Res.</i> <u>52</u> :2389-93;	
		PLUNKETT <i>et al.</i> , Pharmacologically directed ara-C therapy for refractory leukemia, 1985, <i>Semin Oncol</i> <u>12</u> :20-30;	
		RUIZ VAN HAPEREN <i>et al.</i> , Development and molecular characterization of a 2',2'-difluorodeoxycytidine-resistant variant of the human ovarian carcinoma cell line A2780, 1994, <i>Cancer Res.</i> <u>54</u> :4138-43	
		SANDLIE AND BREKKE, Therapeutic antibodies for human diseases at the dawn of the twenty-first century, 2003, <i>Nat. Rev. Drug Discovery</i> <u>2</u> :52-62	
		STEGMANN <i>et al.</i> , Transfection of wild-type deoxycytidine kinase (dck) cDNA into an AraC- and DAC-resistant rat leukemic cell line of clonal origin fully restores drug sensitivity, 1995, <i>Blood</i> <u>85</u> :1188-94	
		VAN ROMPAY, <i>et al.</i> , Phosphorylation of nucleosides and nucleoside analogs by mammalian nucleoside monophosphate kinases, 2000, <i>Pharmacol. Ther.</i> <u>87</u> :189-98	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> Applicant is to place a check mark here if English translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC. 20231